CHILDREN'S ONCOLOGY GROUP

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Guidance on Platelet Transfusion for Patients with Cancer

COG Supportive Care Endorsed Guidelines

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The evidence-based recommendations included in the "Platelet Transfusion for Patients with Cancer: American Society of Clinical Oncology (ASCO) Clinical Practice Guideline Update" were endorsed by the COG Supportive Care Guideline Committee in October, 2018.

The source guideline is published Schiffer CA, Bohlke K, Delaney M, et al. J Clin Oncol. 2018;36(3):283-299. doi:10.1200/JCO.2017.76.1734) and is available at: http://ascopubs.org/doi/pdf/10.1200/JCO.2017.76.1734

The purpose of the source guideline is to provide evidence-based recommendations regarding the use of platelet transfusion in people with cancer. They are limited to people aged 4 months and older.

Recommendations from the endorsed clinical practice guideline are presented in the table below. Recommendations deemed not to be generalizable to pediatric patients by the source clinical practice guideline panel have been omitted.

Summary of Recommendations for Platelet Transfusion for Patients with Cancer

RECOMMENDATIONS	Strength of Recommendation and Quality of Evidence*
How should platelets for transfusion be prepared?	
• Platelets for transfusion can be prepared either by separation of units of platelet concentrates (PCs) from whole blood using either the buffy coat (BC) or the platelet-rich plasma (PRP) method, which can be pooled before administration, or by apheresis from single donors. Comparative studies have shown that the post-transfusion increments, hemostatic benefit, and adverse effects are similar with any of these platelet products. Thus, in routine circumstances, they can be used interchangeably. In most centers, pooled PCs are less costly. Single-donor platelets from selected donors are necessary when histocompatible platelet transfusions are needed. (ASCO Q1)	Evidence quality: High Strength of recommendation: Strong
Should platelet transfusions be given prophylactically or therapeutically?	
• Prophylactic platelet transfusion should be administered to patients with thrombocytopenia resulting from impaired bone marrow function to reduce the risk of hemorrhage when the platelet count falls below a predefined threshold level. This threshold level for transfusion varies according to the patient's diagnosis, clinical condition, and treatment modality. (ASCO Q4)	Evidence quality: High Strength of recommendation: Strong

RECOMMENDATIONS	Strength of Recommendation and Quality of Evidence*
What platelet transfusion threshold should be used?	
• **Patients with Hematologic Malignancies**: The Panel recommends a threshold of <10 x 10^9/L for prophylactic platelet transfusion in patients receiving therapy for hematologic malignancies. Transfusion at higher levels may be advisable in patients with signs of hemorrhage, high fever, hyperleukocytosis, rapid fall of platelet count, or coagulation abnormalities (eg, acute promyelocytic leukemia) and in those undergoing invasive procedures or in circumstances in which platelet transfusions may not be readily available in case of emergencies, as might be the case for outpatients who live at a distance from the treatment center. (ASCO Q5)	Evidence quality: High Strength of recommendation: Strong
• **Patients in the Setting of Hematopoietic Stem Cell Transplant:** The Panel recommends a threshold of < 10 x 10^9/L for prophylactic platelet transfusion in adult and pediatric patients undergoing allogeneic HSCT. Prophylactic platelet transfusion may be administered at higher counts based on clinician judgment. (ASCO Q6)	Evidence quality: High Strength of recommendation: Moderate
• **Platelet Count at which Surgical or Invasive Procedures may be Performed**: The Panel recommends a threshold of 40 x 10^9/L to 50 x 10^9/L for performing major invasive procedures in the absence of associated coagulation abnormalities. Certain procedures, such as bone marrow aspirations and biopsies, and removal of central venous catheters, can be performed safely at counts < 20 x 10^9/L. There are sparse data, and no randomized trials, addressing the safety of other invasive procedures at much lower count levels. If platelet transfusions are administered before a procedure, it is critical that a post-transfusion platelet count be obtained to prove that the desired platelet count level has been reached. Platelet transfusions should also be available on short notice, in case intraoperative or postoperative bleeding occurs. For alloimmunized patients, histocompatible platelets must be available in these circumstances. (ASCO Q9)	Evidence quality: Low Strength of recommendation: Weak

RECOMMENDATIONS	Strength of Recommendation and Quality of Evidence*
In what circumstances should providers take steps to prevent Rh alloimmunization resulting from platelet transfusion?	
• Prevention of RhD alloimmunization resulting from platelet transfusions to RhD-negative recipients can be achieved either through the exclusive use of platelet products collected from RhD-negative donors or via anti-D immune prophylaxis. These approaches may be used for female children and female adults of child-bearing potential being treated with curative intent. However, because of the low rate of RhD alloimmunization in patients with cancer, these approaches need not be applied universally. (ASCO Q2)	Evidence quality: Intermediate Strength of recommendation: Moderate
How should refractoriness to platelet transfusion be managed?	
Implementation tip from the COG Supportive Care Guideline Committee: The recommendation below applies to platelet refractoriness due to alloimmunization. Other causes of platelet refractoriness should be excluded.	
• Alloimmunization is usually due to antibody against HLA antigens and only rarely to platelet-specific antigens. Patients with alloimmune-refractory thrombocytopenia, as defined previously,† are best managed with platelet transfusions from histocompatible donors matched for HLA-A and HLA-B antigens. Many blood suppliers have access to computerized lists of such donors. For patients (1) whose HLA type cannot be determined, (2) who have uncommon HLA types for whom suitable donors cannot be identified, or (3) who do not respond to HLA-matched platelets, histocompatible platelet donors can often be identified using platelet cross-matching techniques. In many patients, these two techniques are complementary. (ASCO Q11) †A diagnosis of refractoriness to platelet transfusion should be made only when at least two transfusions of ABO-compatible units, stored for < 72 hours, result in poor increments. See: Schiffer CA, et al. J Clin Oncol. 2018; 36(3):283-99.	Evidence quality: High Strength of recommendation: Strong

RECOMMENDATIONS	Strength of Recommendation and Quality of Evidence*
In what circumstances should providers use leukoreduced blood products to prevent alloimmunization?	
• The incidence of alloantibody-mediated refractoriness to platelet transfusion can be decreased in patients with acute myeloid leukemia (AML) receiving induction chemotherapy when both platelet and RBC products are leukoreduced before transfusion. It is therefore appropriate to provide leukoreduced blood products to patients with AML from the time of diagnosis to ameliorate this important clinical problem. Although randomized trials have not been conducted in other patient groups, it is likely that alloimmunization can also be decreased in patients with other types of leukemia and in other patients with cancer who are receiving chemotherapy. There are fewer data in patients who are not receiving chemotherapy in the same time periods that the transfusions are being administered (eg, aplastic anemia, myelodysplasia), although the consensus would favor its use in these patients as well. In the United States and in several other countries, the overwhelming majority of blood products are now leukoreduced at the time of blood collection and component preparation. Other advantages of prestorage leukoreduction include a substantial reduction in transfusion reactions and in transmission of cytomegalovirus infection. (ASCO Q3)	Evidence quality: High Strength of recommendation: Strong

*see Appendix 1

Appendix 1: Systems for Classifying Recommendations and Evidence used by the Source Clinical Practice Guidelines

American Society of Clinical Oncology: Schiffer CA, Bohlke K, Delaney M, et al. Platelet Transfusion for Patients With Cancer: American Society of Clinical Oncology Clinical Practice Guideline Update. J Clin Oncol. 2018; 36(3):283-299. Data supplement.

Guide for Strength of Recommendations

Rating for Strength of Recommendation	Definition
Strong	There is high confidence that the recommendation reflects best practice. This is based on (1) strong evidence for a true net effect (eg, benefits exceed harms); (2) consistent results, with no or minor exceptions; (3) minor or no concerns about study quality; and/or (4) the extent of Expert Panelists' agreement. Other compelling considerations (discussed in the guideline's literature review and analyses) may also warrant a strong recommendation.
Moderate	There is moderate confidence that the recommendation reflects best practice. This is based on (1) good evidence for a true net effect (eg, benefits exceed harms); (2) consistent results, with minor and/or few exceptions; (3) minor and/or few concerns about study quality; and/or (4) the extent of Expert Panelists' agreement. Other compelling considerations (discussed in the guideline's literature review and analyses) may also warrant a moderate recommendation.
Weak	There is some confidence that the recommendation offers the best current guidance for practice. This is based on (1) limited evidence for a true net effect (eg, benefits exceed harms); (2) consistent results, but with important exceptions; (3) concerns about study quality; and/or (4) the extent of Expert Panelists' agreement. Other considerations (discussed in the guideline's literature review and analyses) may also warrant a weak recommendation.

Guide for Strength of Evidence

Rating for Strength of Evidence	Definition
High	High confidence that the available evidence reflects the true magnitude and direction of the net effect (i.e., balance of benefits *v* harms) and that further research is very unlikely to change either the magnitude or direction of this net effect.
Intermediate	Moderate confidence that the available evidence reflects the true magnitude and direction of the net effect. Further research is unlikely to alter the direction of the net effect; however, it might alter the magnitude of the net effect.
Low	Low confidence that the available evidence reflects the true magnitude and direction of the net effect. Further research may change either the magnitude and/or direction this net effect.
Insufficient	Evidence is insufficient to discern the true magnitude and direction of the net effect. Further research may better inform the topic. The use of the consensus opinion of experts is reasonable to inform outcomes related to the topic.